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(71) Applicant
Inpharzam International S.A.

(Incorporated in Switzerland)

PO Box 6812, CH-6814 Cadempino, Switzerland

(72) Inventors
Annibale Gazzaniga
Valter Gianesello
Federico Stroppolo

(74) Agent and/or Address for Service
Serjeants,
25 The Crescent, King Street, Leicester LE1 6RX

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(54) Acetylcysteine compositions

(57) A pharmaceutical composition in the form of water-soluble granules comprises:

N-Acetylcysteine	10–20%	by weight
Aspartame	2 – 3%	by weight
Sorbitol	67–78%	by weight
Flavouring Agent	About 10%	by weight

The composition has mucolytic activity, is non-cariogenic, and suitable for diabetics.

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SPECIFICATION

Pharmaceutical compositions

The invention relates to pharmaceutical compositions containing N-acetylcysteine.

N-acetylcysteine (hereinafter designated NAC) is a medicament with diverse favourable properties, one of which is mucolytic activity. For use in practice as a mucolytic agent, NAC can be taken orally in the form of an aqueous solution obtained by dissolving effervescent granules or an effervescent tablet. The organoleptic properties of the medicament can, however, be subjectively unpleasant. It is therefore necessary to lessen the typical taste of NAC in the case of oral administration.

In the pharmaceutical forms currently available commercially this is accomplished by an addition of sucrose. However, the use of sucrose can have disadvantages, especially for persons who suffer from diabetes. In addition, sucrose is a cariogenic sugar. It is therefore necessary to be able to provide, as an alternative to the already existing pharmaceutical forms, novel pharmaceutical preparations of NAC for oral use, which are indicated for subjects to whom sucrose can be harmful. The substitution of sucrose by an artificial sweetener or a non-cariogenic sweetening agent in a pharmaceutical form containing NAC is a problem which at first sight would appear easy to solve. In reality, there are manifold problems which are difficult to solve.

For example, it is necessary that the NAC and the sweetener are chemically compatible, that the sweetener or sweetening agent is capable of effectively masking or lessening the typical flavour of NAC, that the resulting taste is pleasant anyhow, that the sweetener or sweetening agent is suitable for preparing the desired pharmaceutical form and is compatible with the associated operations.

The invention provides a pharmaceutical composition in the form of water soluble granules, the composition comprising from 10 to 20% by weight of N-acetylcysteine, from 2 to 3% by weight of aspartame, from 67 to 75% by weight of sorbitol and about 10% by weight of a pharmaceutically acceptable flavouring agent.

The flavouring agent is suitably present in an amount of from 5 to 15%, preferably 10% by weight.

Having regard to the acceptability by the consumer of the medicament, the use of a flavouring agent may demand the presence of acolourant which is normally associated with a particular taste. For example, the use of mint flavouring can demand the addition of a colourant which imparts a green colour to the solution. In such cases, it can be useful to combine the composition with a quantity of a pharmaceutically acceptable colourant, for example in a quantity between 0.5 and 1% by weight.

The granules according to the invention are prepared by procedures usual in pharmaceutical operations.

The granules can be distributed in suitable sachets containing, for example, 1, 1.5 or 2 g of the composition.

Preferably, each sachet contains a quantity of the composition corresponding to 100, 150, 200 or 300 mg of NAC.

With reference to a dose of 1 g, representative examples of granules according to the invention are as follows:

- NAC	100	mg
Aspartame	25	mg
Sorbitol	775	mg
Lemon flavouring	100	mg
- NAC	100	mg
Aspartame	25	mg
Sorbitol	774.2	mg
Mint flavouring	100	mg
Green colourant	0.8	mg
- NAC	200	mg
Aspartame	25	mg
Sorbitol	675	mg
Lemon flavouring	100	mg
- NAC	200	mg
Aspartame	25	mg
Sorbitol	674.2	mg
Orange flavouring	100	mg
Orange colourant (or β-carotene)	0.8	mg
- NAC	150	mg
Aspartame	30	mg
Sorbitol	720	mg
Citrus fruit flavouring	100	mg

The granules according to the invention disolve rapidly in water, giving an aqueous solution of NAC of pleasant palatability. The following Examples illustrate the invention.

Example 1

Granules composed of

NAC	10	kg
Aspartame	2.5	kg
Sorbitol	77.42	kg
Orange flavouring	10	kg
Colourant E110	0.08	kg

are prepared by the following procedure.

The powders, excepting the colourant, are sieved through a screen of 1.07 mm mesh width and mixed for ten minutes. The mixture is then granulated in a fluid-bed granulator with an aqueous solution of the colourant.

The granules are then distributed over blisters in a laminated aluminium-polyethylene sheet in a dose of 1 g per blister (NAC dose per blister = 100 mg).

Example 2

Blisters containing 1 g of the composition(NAC content = 200 mg) are prepared in a manner

analogous to that described in Example 1, but starting from

NAC	20	kg
Aspartame	2.5	kg
Sorbitol	67.42	kg
Orange flavouring	10	kg
β-carotene	0.08	kg

Example 3

Granules comprising

NAC	15	kg
Aspartame	3	kg
Sorbitol	72	kg
Citrus fruit flavouring	10	kg

are prepared in a manner analogous to that described in Example 1, but without the use of colourant.

The granules are distributed over blisters in a laminated aluminium/polyethylene sheet in a dose of 2 g per blister (300 mg of NAC per dose) or in an alternative dose of 1 g per blister (150 mg of NAC per dose).

Example 4

The composition described in Example 1 may also be prepared by the following alternative procedure.

The NAC, the sorbitol and the aspartame are sieved on a vibrating screen of 1.08 mm mesh width and mixed. The mixture is placed in an autogranulator and granulated with an aqueous solution containing colourant E.110. The granules obtained are dried in the fixed bed (oven) and then homogenised by means of a vibrating granulator equipped with a screen of 1.0 mm mesh width. The flavouring is added during granulation and the whole is then mixed again until a homogeneous mixture is obtained.

The mixture is distributed over blisters in a laminated aluminium/polyethylene sheet in a dose of 1 g per blister (100 mg of NAC per dose).

Example 5

The composition described in Example 2 may also be prepared by the following alternative method.

The NAC, the sorbitol and the aspartame are sieved through a vibrating screen of 1.08 mm mesh width and mixed. The mixture is placed in a fluid-bed autogranulator and granulated with an aqueous:alcoholic (1:1) solution containing the B-carotene. The dried granules are homogenised by means of a 1.08 mm screen and mixed with the orange flavouring. The mixture is then distributed over blisters in a laminated aluminium/polyethylene sheet in a dose of 1 g per blister (200 mg of NAC per dose).

CLAIMS

1. A pharmaceutical composition in the form of water soluble granules, the composition comprising from 10 to 20% by weight of N-acetylcysteine, from 2 to 3% by weight of aspartame, from 67 to 78% by weight of sorbitol and about 10% by weight of a pharmaceutically acceptable flavouring agent.

2. A pharmaceutical composition according to Claim 1 containing a quantity selected from 100, 150, 200 and 300 mg of N-acetylcysteine per single dose.

3. A pharmaceutical composition according to Claim 1 or Claim 2 further comprising a pharmaceutically acceptable colourant.

4. A pharmaceutical composition according to Claim 1 or Claim 2 and comprising:

N-Acetylcysteine	10% by weight
Aspartame	2.5% by weight
Sorbitol	77.5% by weight
Flavouring Agent	10% by weight

5. A pharmaceutical composition according to Claim 1 or Claim 2 and comprising:

N-Acetylcysteine	20% by weight
Aspartame	2.5% by weight
Sorbitol	67.5% by weight
Flavouring Agent	10% by weight

6. A pharmaceutical composition according to Claim 3 and comprising:

N-Acetylcysteine	10% by weight
Aspartame	2.5% by weight
Sorbitol	77.42% by weight
Flavouring Agent	10% by weight
Colourant	0.08% by weight

7. A pharmaceutical composition according to Claim 3 and comprising:

N-Acetylcysteine	20% by weight
Aspartame	2.5% by weight
Sorbitol	67.42% by weight
Flavouring Agent	10% by weight
Colourant	0.08% by weight

8. A pharmaceutical composition according to Claim 1 or Claim 2 and comprising:

N-Acetylcysteine	15% by weight
Aspartame	3% by weight
Sorbitol	72% by weight
Flavouring Agent	10% by weight

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